

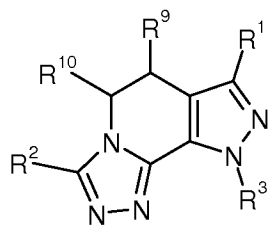
## **Listing of Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**1. (Currently Amended)** A composition comprising a carrier and, *(I)* a PDE4 inhibitor and *(II)* an anti-cholinergic agent selected from the group consisting of tiotropium, ~~and pharmaceutically acceptable salts, isomers, isotopes, polymorphs, hydrates and solvates thereof~~, a pharmaceutically acceptable salt of tiotropium, an isomer of tiotropium, an isotope of tiotropium, a polymorph of tiotropium, a hydrate of tiotropium, and a solvate of tiotropium, in an effective therapeutic amount to treat an inflammatory disease or obstructive airways disease.

**2. (Original)** The composition according to claim 1 wherein said obstructive airways disease is asthma, COPD, or other obstructive airways disease exacerbated by bronchial hyper-reactivity or bronchospasm.

**3. (Currently Amended)** The composition according to claim 1 wherein said PDE4 inhibitor is a compound of Formula (1.1.1):

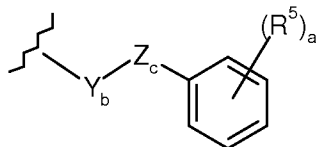


(1.1.1)

wherein:

$R^1$  is  $-H$ ;  $(C_1-C_6)$  alkyl;  $(C_1-C_6)$  alkoxy;  $(C_2-C_4)$  alkenyl; phenyl;  $-N(CH_3)_2$ ;  $(C_3-C_6)$  cycloalkyl;  $(C_3-C_6)$  cycloalkyl- $(C_1-C_3)$  alkyl; or  $(C_1-C_6)$  alkylcarbonyl; where said alkyl, phenyl or alkenyl group is substituted by 0 to 2 of  $-OH$ ,  $(C_1-C_3)$  alkyl, or  $-CF_3$ , or 0 to 3 of halo;

$R^2$  and  $R^3$  are each independently selected from the group consisting of:  $-H$ ;  $(C_1-C_{14})$  alkyl;  $(C_1-C_7)$  alkoxy- $(C_1-C_7)$  alkyl;  $(C_2-C_{14})$  alkenyl;  $(C_3-C_7)$  cycloalkyl;  $(C_3-C_7)$  cycloalkyl- $(C_1-C_2)$  alkyl; a saturated or unsaturated  $(C_4-C_7)$  heterocyclic- $(CH_2)_n$  group where  $n$  is 0, 1 or 2, containing as the heteroatom one or two ~~of~~ atoms or groups selected from the group consisting of oxygen, sulfur, sulfonyl, nitrogen and  $NR^4$  where  $R^4$  is  $-H$  or  $(C_1-C_4)$  alkyl; and a group of partial Formula (1.1.2):



(1.1.2)

where

$a$  is an integer from 1 to 5;

$b$  and  $c$  are 0 or 1;

$R^5$  is  $-H$ ;  $-OH$ ;  $(C_1-C_5)$  alkyl;  $(C_2-C_5)$  alkenyl;  $(C_1-C_5)$  alkoxy;  $(C_3-C_6)$  cycloalkoxy; halo;  $-CF_3$ ;  $-CO_2R^6$ ;  $-CONR^6R^7$ ;  $-NR^6R^7$ ;  $-NO_2$ ; or  $-SO_2NR^6R^7$  where  $R^6$  and  $R^7$  are each independently  $-H$ ; or  $(C_1-C_4)$  alkyl;

$Z$  is  $-O-$ ;  $-S-$ ;  $-SO_2-$ ;  $-C(=O)-$ ; or  $-N(R^8)-$  where  $R^8$  is  $-H$ ; or  $(C_1-C_4)$  alkyl; and

$Y$  is  $(C_1-C_5)$  alkylene; or  $(C_2-C_6)$  alkenylene; each substituted by 0 to 2 of  $(C_1-C_7)$  alkyl or  $(C_3-C_7)$  cycloalkyl; and

wherein each of said above-recited alkyl, alkenyl, cycloalkyl, alkoxyalkyl or heterocyclic groups is substituted by 0 to 14, ~~preferably 0 to 5~~, of (C<sub>1</sub>-C<sub>2</sub>) alkyl, CF<sub>3</sub>, or halo; and

R<sup>9</sup> and R<sup>10</sup> are each independently selected from the group consisting of -H; (C<sub>1</sub>-C<sub>6</sub>) alkyl; (C<sub>1</sub>-C<sub>6</sub>) alkoxy; (C<sub>6</sub>-C<sub>10</sub>) aryl; and (C<sub>6</sub>-C<sub>10</sub>) aryloxy;

or a pharmaceutically acceptable salt thereof.

**4. (Currently Amended)** The composition according to claim 3 wherein the PDE4 inhibitor ~~comprises a member~~ is selected from the group consisting of:

9-cyclopentyl-5,6-dihydro-7-ethyl-3-phenyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(furan-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(4-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(3-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-benzyl-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-propyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3,9-dicyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-(*tert*-butyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methoxyphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-(2-chlorophenyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

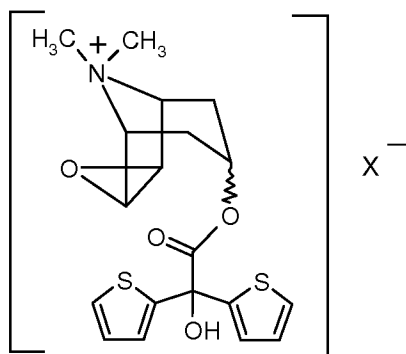
9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-iodophenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-trifluoromethylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine; and

5,6-dihydro-7-ethyl-9-(4-fluorophenyl)-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine.

**5. (Currently Amended)** The composition according to claim 3 wherein the PDE4 inhibitor is ~~9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine or 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine~~ 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine or 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(*tert*-butyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine.

**6. (Currently Amended)** The composition according to claim 1 wherein the anti-cholinergic agent ~~comprises a member is selected from the group consisting of tiotropium, and pharmaceutically acceptable salts, isomers, isotopes, polymorphs, hydrates and solvates thereof, and a tiotropium~~ compound of Formula (2.1.1):



(2.1.1)

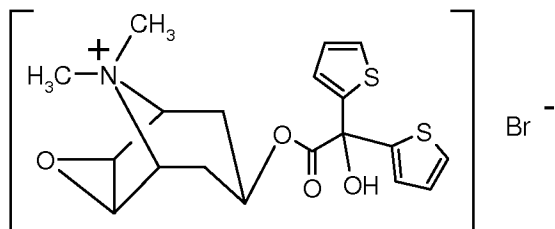
wherein  $X^-$  is a physiologically acceptable anion.

**7. (Original)** The composition according to claim 6 wherein said physiologically acceptable anion,  $X^-$ , is selected from the group consisting of fluoride,  $F^-$ ; chloride,  $Cl^-$ ; bromide,  $Br^-$ ; iodide,  $I^-$ ; methanesulfonate,  $CH_3S(=O)_2O^-$ ; ethanesulfonate,  $CH_3CH_2S(=O)_2O^-$ ; methylsulfate,  $CH_3OS(=O)_2O^-$ ; benzene sulfonate,  $C_6H_5S(=O)_2O^-$ ; *p*-toluenesulfonate, and 4- $CH_3-C_6H_4S(=O)_2O^-$ .

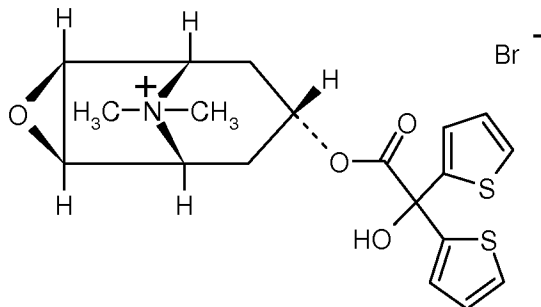
**8. (Original)** The composition according to claim 7 wherein the physiologically acceptable anion,  $X^-$ , is bromide,  $Br^-$ .

**9. (Currently Amended)** The composition according to claim 6 wherein the anti-cholinergic agent comprises a 3- $\alpha$  tiotropium compound.

**10. (Currently Amended)** The composition according to ~~claim 9~~ claim 1 wherein the anti-cholinergic agent is selected from the group consisting of tiotropium bromide and (1 $\alpha$ , 2 $\beta$ , 4 $\beta$ , 5 $\beta$ , 7 $\beta$ )-7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-3-oxa-9-azoniatricyclo[3.3.1.0<sup>2,4</sup>]nonane bromide, represented by Formula (2.1.2) or Formula (2.1.3):



(2.1.2)



(2.1.3)

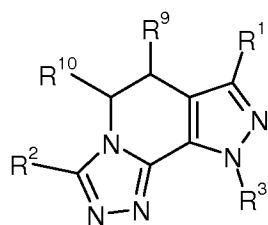
**11. (Withdrawn-Currently Amended)** A method for the treatment of an obstructive airways or inflammatory disease, comprising administering to a mammal (I) a PDE4 inhibitor and, (II) an anti-cholinergic agent ~~comprising a member~~ selected from the group consisting of tiotropium and ~~a pharmaceutically acceptable salts, isomers, isotopes, polymorphs, hydrates and solvates thereof~~, a pharmaceutically acceptable salt of tiotropium, an isomer of tiotropium, an isotope of tiotropium, a polymorph of tiotropium, a hydrate of tiotropium, and a solvate of tiotropium, in a therapeutically effective amount to treat the disease when administered by inhalation.

**12. (Withdrawn)** The method according to claim 11 wherein the obstructive airways disease is asthma, COPD, or other obstructive airways disease exacerbated by bronchial hyper-reactivity or bronchospasm.

**13. (Withdrawn)** The method of treatment according to claim 12 wherein the mammal is a human being.

**14. (Withdrawn)** The method according to claim 11 wherein the administration comprises simultaneous or sequential delivery of the PDE4 inhibitor and anti-cholinergic agent in the form of an aerosol or dry powder.

**15. (Withdrawn-Currently Amended)** The method according to claim 11 wherein the PDE4 inhibitor comprises a compound of Formula (1.1.1):



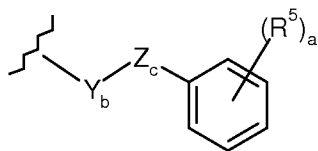
(1.1.1)

wherein:

R<sup>1</sup> is -H; (C<sub>1</sub>-C<sub>6</sub>) alkyl; (C<sub>1</sub>-C<sub>6</sub>) alkoxy; (C<sub>2</sub>-C<sub>4</sub>) alkenyl; phenyl; -N(CH<sub>3</sub>)<sub>2</sub>; (C<sub>3</sub>-C<sub>6</sub>) cycloalkyl; (C<sub>3</sub>-C<sub>6</sub>) cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>) alkyl; or (C<sub>1</sub>-C<sub>6</sub>) alkylcarbonyl; where said alkyl, phenyl or alkenyl group is substituted by 0 to 2 of -OH, (C<sub>1</sub>-C<sub>3</sub>) alkyl, or -CF<sub>3</sub>, or 0 to 3 of halo;

R<sup>2</sup> and R<sup>3</sup> are each independently selected from the group consisting of: -H; (C<sub>1</sub>-C<sub>14</sub>) alkyl; (C<sub>1</sub>-C<sub>7</sub>) alkoxy-(C<sub>1</sub>-C<sub>7</sub>) alkyl; (C<sub>2</sub>-C<sub>14</sub>) alkenyl; (C<sub>3</sub>-C<sub>7</sub>) cycloalkyl;

(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl-(C<sub>1</sub>-C<sub>2</sub>) alkyl; a saturated or unsaturated (C<sub>4</sub>-C<sub>7</sub>) heterocyclic-(CH<sub>2</sub>)<sub>n</sub> group where n is 0, 1 or 2, containing as the heteroatom one or two of atoms or groups selected from the group consisting of oxygen, sulfur, sulfonyl, nitrogen and NR<sup>4</sup> where R<sup>4</sup> is -H or (C<sub>1</sub>-C<sub>4</sub>) alkyl; and a group of partial Formula (1.1.2):



(1.1.2)

where

a is an integer from 1 to 5;

b and c are 0 or 1;

R<sup>5</sup> is -H; -OH; (C<sub>1</sub>-C<sub>5</sub>) alkyl; (C<sub>2</sub>-C<sub>5</sub>) alkenyl; (C<sub>1</sub>-C<sub>5</sub>) alkoxy; (C<sub>3</sub>-C<sub>6</sub>) cycloalkoxy; halo; -CF<sub>3</sub>; -CO<sub>2</sub>R<sup>6</sup>; -CONR<sup>6</sup>R<sup>7</sup>; -NR<sup>6</sup>R<sup>7</sup>; -NO<sub>2</sub>; or -SO<sub>2</sub>NR<sup>6</sup>R<sup>7</sup> where R<sup>6</sup> and R<sup>7</sup> are each independently -H; or (C<sub>1</sub>-C<sub>4</sub>) alkyl;

Z is -O-; -S-; -SO<sub>2</sub>-; -C(=O)-; or -N(R<sup>8</sup>)- where R<sup>8</sup> is -H; or (C<sub>1</sub>-C<sub>4</sub>) alkyl; and

Y is (C<sub>1</sub>-C<sub>5</sub>) alkylene; or (C<sub>2</sub>-C<sub>6</sub>) alkenylene; each substituted by 0 to 2 of (C<sub>1</sub>-C<sub>7</sub>) alkyl or (C<sub>3</sub>-C<sub>7</sub>) cycloalkyl; and

wherein each of said above-recited alkyl, alkenyl, cycloalkyl, alkoxyalkyl or heterocyclic groups is substituted by 0 to 14, ~~preferably 0 to 5~~, of (C<sub>1</sub>-C<sub>2</sub>) alkyl, CF<sub>3</sub>, or halo; and

R<sup>9</sup> and R<sup>10</sup> are each independently selected from the group consisting of -H; (C<sub>1</sub>-C<sub>6</sub>) alkyl; (C<sub>1</sub>-C<sub>6</sub>) alkoxy; (C<sub>6</sub>-C<sub>10</sub>) aryl; and (C<sub>6</sub>-C<sub>10</sub>) aryloxy;



or a pharmaceutically acceptable salt thereof.

**16. (Withdrawn-Currently Amended)** The method according to claim 15 wherein the PDE4 inhibitor ~~comprises a member~~ is selected from the group consisting of:

9-cyclopentyl-5,6-dihydro-7-ethyl-3-phenyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(furan-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(4-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(3-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-benzyl-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-propyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3,9-dicyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-(*tert*-butyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methoxyphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9*H*-pyrazolo[3,4-*c*]1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

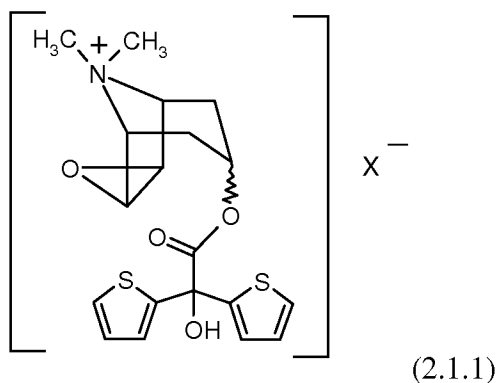
3-(2-chlorophenyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-iodophenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-trifluoromethylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine; and

5,6-dihydro-7-ethyl-9-(4-fluorophenyl)-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine.

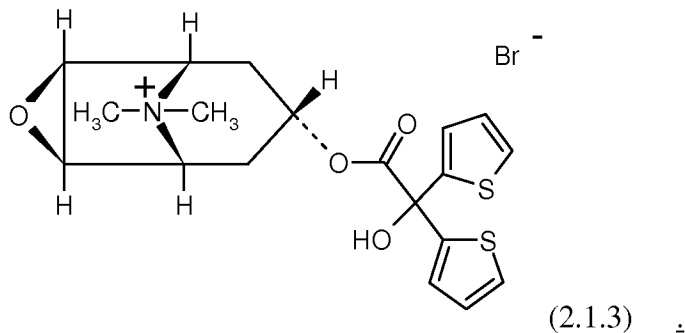
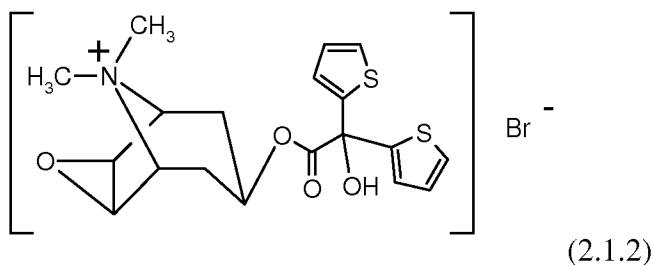
**17. (Withdrawn-Currently Amended)** The method according to claim 11 wherein the anti-cholinergic agent comprises ~~a member selected from the group consisting of tiotropium, and pharmaceutically acceptable salts, isomers, isotopes, polymorphs, hydrates and solvates thereof, and is a tiotropium~~ compound of Formula (2.1.1):



wherein  $X^-$  is a physiologically acceptable anion.

**18. (Withdrawn)** The method according to claim 17 wherein the physiologically acceptable anion,  $X^-$ , is bromide,  $Br^-$ .

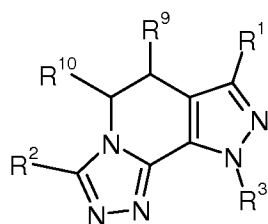
**19. (Withdrawn-Currently Amended)** A method of treatment according to ~~claim 18~~ claim 11 wherein the anti-cholinergic agent ~~comprises a~~ is selected from the group consisting of tiotropium bromide and (1 $\alpha$ , 2 $\beta$ , 4 $\beta$ , 5 $\beta$ , 7 $\beta$ )-7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-3-oxa-9-azoniatricyclo[3.3.1.0<sup>2,4</sup>]nonane bromide, represented by Formula (2.1.2) or Formula (2.1.3):



**20. (Original)** The composition according to claim 1 comprising a carrier, (I) a PDE4 inhibitor and, (II) an anticholinergic agent, in a form suitable for administration by inhalation.

**21. (Currently Amended)** The composition according to claim 20 wherein the form suitable for administration by inhalation comprises simultaneous or ~~sequential delivery of~~ sequentially deliverable forms of components (I) and (II) in the form of an aerosol or dry powder.

**22. (Currently Amended)** The composition according to claim 20 wherein the PDE4 inhibitor comprises a compound of formula (1.1.1)



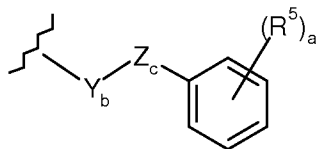
(1.1.1)

wherein:

$R^1$  is -H; (C<sub>1</sub>-C<sub>6</sub>) alkyl; (C<sub>1</sub>-C<sub>6</sub>) alkoxy; (C<sub>2</sub>-C<sub>4</sub>) alkenyl; phenyl; -N(CH<sub>3</sub>)<sub>2</sub>; (C<sub>3</sub>-C<sub>6</sub>) cycloalkyl; (C<sub>3</sub>-C<sub>6</sub>) cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>) alkyl; or (C<sub>1</sub>-C<sub>6</sub>) alkylcarbonyl; where said alkyl, phenyl or alkenyl group is substituted by 0 to 2 of -OH, (C<sub>1</sub>-C<sub>3</sub>) alkyl, or -CF<sub>3</sub>, or 0 to 3 of halo;

$R^2$  and  $R^3$  are each independently selected from the group consisting of: -H; (C<sub>1</sub>-C<sub>14</sub>) alkyl; (C<sub>1</sub>-C<sub>7</sub>) alkoxy-(C<sub>1</sub>-C<sub>7</sub>) alkyl; (C<sub>2</sub>-C<sub>14</sub>) alkenyl; (C<sub>3</sub>-C<sub>7</sub>) cycloalkyl; (C<sub>3</sub>-C<sub>7</sub>) cycloalkyl-(C<sub>1</sub>-C<sub>2</sub>) alkyl; a saturated or unsaturated (C<sub>4</sub>-C<sub>7</sub>) heterocyclic-(CH<sub>2</sub>)<sub>n</sub> group where n is 0, 1 or 2, containing as the heteroatom one or two of atoms or groups

selected from the group consisting of oxygen, sulfur, sulfonyl, nitrogen and  $\text{NR}^4$  where  $\text{R}^4$  is  $-\text{H}$  or  $(\text{C}_1\text{-C}_4)$  alkyl; and a group of partial Formula (1.1.2):



(1.1.2)

where

a is an integer from 1 to 5;

b and c are 0 or 1;

$\text{R}^5$  is  $-\text{H}$ ;  $-\text{OH}$ ;  $(\text{C}_1\text{-C}_5)$  alkyl;  $(\text{C}_2\text{-C}_5)$  alkenyl;  $(\text{C}_1\text{-C}_5)$  alkoxy;  $(\text{C}_3\text{-C}_6)$  cycloalkoxy; halo;  $-\text{CF}_3$ ;  $-\text{CO}_2\text{R}^6$ ;  $-\text{CONR}^6\text{R}^7$ ;  $-\text{NR}^6\text{R}^7$ ;  $-\text{NO}_2$ ; or  $-\text{SO}_2\text{NR}^6\text{R}^7$  where  $\text{R}^6$  and  $\text{R}^7$  are each independently  $-\text{H}$ ; or  $(\text{C}_1\text{-C}_4)$  alkyl;

Z is  $-\text{O}-$ ;  $-\text{S}-$ ;  $-\text{SO}_2-$ ;  $-\text{C}(=\text{O})-$ ; or  $-\text{N}(\text{R}^8)-$  where  $\text{R}^8$  is  $-\text{H}$ ; or  $(\text{C}_1\text{-C}_4)$  alkyl; and

Y is  $(\text{C}_1\text{-C}_5)$  alkylene; or  $(\text{C}_2\text{-C}_6)$  alkenylene; each substituted by 0 to 2 of  $(\text{C}_1\text{-C}_7)$  alkyl or  $(\text{C}_3\text{-C}_7)$  cycloalkyl; and

wherein each of said above-recited alkyl, alkenyl, cycloalkyl, alkoxyalkyl or heterocyclic groups is substituted by 0 to 14, ~~preferably 0 to 5~~, of  $(\text{C}_1\text{-C}_2)$  alkyl,  $\text{CF}_3$ , or halo; and

$\text{R}^9$  and  $\text{R}^{10}$  are each independently selected from the group consisting of  $-\text{H}$ ;  $(\text{C}_1\text{-C}_6)$  alkyl;  $(\text{C}_1\text{-C}_6)$  alkoxy;  $(\text{C}_6\text{-C}_{10})$  aryl; and  $(\text{C}_6\text{-C}_{10})$  aryloxy; or a pharmaceutically acceptable salt thereof.

**23. (Original)** The composition according to claim 22 wherein the PDE4 inhibitor comprises a compound selected from the group consisting of

9-cyclopentyl-5,6-dihydro-7-ethyl-3-phenyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(furan-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(4-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(3-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-benzyl-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-propyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3,9-dicyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-(*tert*-butyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methoxyphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9*H*-pyrazolo[3,4-*c*]1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

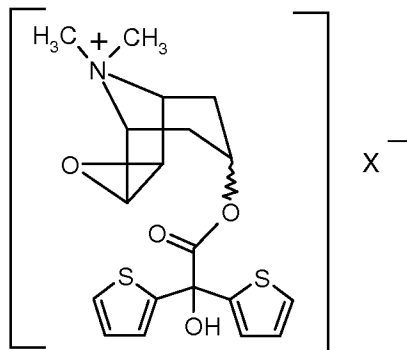
3-(2-chlorophenyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-iodophenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-trifluoromethylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine; and

5,6-dihydro-7-ethyl-9-(4-fluorophenyl)-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine.

**24. (Original)** The composition according to claim 20 wherein the anticholinergic agent comprises a compound of Formula (2.1.1)



(2.1.1)

wherein X<sup>-</sup> is a physiologically acceptable anion.

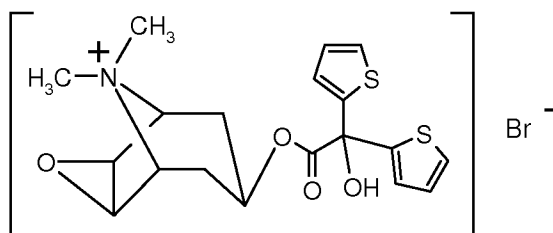
**25. (Original)** The composition according to claim 24 wherein said physiologically acceptable anion, X<sup>-</sup>, is selected from the group consisting of fluoride, F<sup>-</sup>; chloride, Cl<sup>-</sup>; bromide, Br<sup>-</sup>; iodide, I<sup>-</sup>; methanesulfonate, CH<sub>3</sub>S(=O)<sub>2</sub>O<sup>-</sup>; ethanesulfonate,

$\text{CH}_3\text{CH}_2\text{S}(=\text{O})_2\text{O}^-$ ; methylsulfate,  $\text{CH}_3\text{OS}(=\text{O})_2\text{O}^-$ ; benzene sulfonate,  $\text{C}_6\text{H}_5\text{S}(=\text{O})_2\text{O}^-$ ; *p*-toluenesulfonate, and  $4\text{-CH}_3\text{-C}_6\text{H}_4\text{S}(=\text{O})_2\text{O}^-$ .

**26. (Original)** The composition according to claim 25 wherein said physiologically acceptable anion,  $\text{X}^-$ , is bromide,  $\text{Br}^-$ .

**27. (Currently Amended)** The composition according to claim 24 wherein the anticholinergic agent comprises a 3- $\alpha$  tiotropium compound.

**28. (Currently Amended)** The composition according to ~~claim 27~~ claim 24 wherein the anticholinergic agent is selected from the group consisting of tiotropium bromide and (1 $\alpha$ , 2 $\beta$ , 4 $\beta$ , 5 $\beta$ , 7 $\beta$ )-7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-3-oxa-9-azoniatricyclo[3.3.1.0<sup>2,4</sup>]non-ane bromide, represented by Formula (2.1.2):



(2.1.2) <sub>2</sub>

**29. (Currently Amended)** A package containing the composition according to claim 20 capable of insertion into a device for simultaneous or sequential delivery of the composition in the form of an aerosol or dry powder.

**30. (Original)** The package according to claim 29 wherein the composition comprises a PDE4 inhibitor selected from the group consisting of:



9-cyclopentyl-5,6-dihydro-7-ethyl-3-phenyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(furan-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(4-pyridyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(3-thienyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-benzyl-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-propyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3,9-dicyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

3-(*tert*-butyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-methoxyphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(thien-2-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

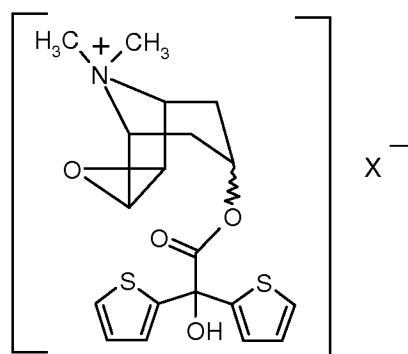
3-(2-chlorophenyl)-9-cyclopentyl-5,6-dihydro-7-ethyl-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-iodophenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine;

9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-trifluoromethylphenyl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine; and

5,6-dihydro-7-ethyl-9-(4-fluorophenyl)-3-(1-methylcyclohex-1-yl)-9*H*-pyrazolo[3,4-*c*]-1,2,4-triazolo[4,3- $\alpha$ ]pyridine.

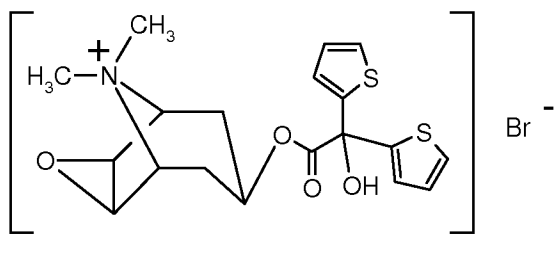
**31. (Original)** The package according to claim 29 wherein the composition comprises an anticholinergic agent of Formula (2.1.1)



wherein  $X^-$  is a physiologically acceptable anion.

**32. (Original)** The package according to claim 31 wherein the physiologically acceptable anion,  $X^-$ , is bromide,  $Br^-$ .

**33. (Currently Amended)** The package according to claim 29 wherein the composition comprises an anticholinergic agent selected from the group consisting of tiotropium bromide and (1 $\alpha$ , 2 $\beta$ , 4 $\beta$ , 5 $\beta$ , 7 $\beta$ )-7-[(hydroxydi-2-thienylacetyl)oxy]-9,9-dimethyl-3-oxa--9-azoniatricyclo[3.3.1.0<sup>2,4</sup>]non-ane bromide, represented by Formula (2.1.2):



**34. (Original)** The package according to claim 29 wherein said device is a metered dose inhaler or a dry powder inhaler.